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EXAMINER	
CROW, ROBERT THOMAS	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,507	YAMAMOTO, NOBUKO	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *15-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/07; 11/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 28 May 2008 is acknowledged.

2. Claims 15-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 28 May 2008.

3. Claims 1-14 are under prosecution.

Information Disclosure Statement

4. The Information Disclosure Statements filed 30 November 2006 and 1 May 2007 are acknowledged. However, only the Abstracts of Documents 2001-522998, 2001-511361, and 11-187900 are being considered because English language translations of the remainder of the documents have not been provided.

Claim Objections

5. Claims 8, 11, and 12 are each objected to because of the following informalities:

A. Claim 8 recites "in human" in line 3, which appears to be a typographical error.

B. Claim 11 recites "are differ" in line 2, which appears to be a typographical error.

C. Claim 12 recites "an same area" a the end of the claim, which appears to be a typographical error.

D. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3, 6-8 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in the recitation "the amount of probes in the plurality of areas varies respectively depending on a target substance to be detected" at the end of the claim. The recitation is indefinite because the amount of probes depends on the amount of target, which is not a structural limitation of the claimed carrier. Thus, it is unclear if a carrier having multiple areas of amounts of probes against a novel set of targets thereon in accordance with claim 3 would be infringed upon merely because different sample of a target substance is isolated that happens to have more of an amount of the target substance than a different sample having less of the target sample.

Claims 6-8 are indefinite in claim 6, which recited the limitation "the probe" in line 2. The singular recitation of "the probe" lacks antecedent basis in the in the plural

recitation of "probes" found in claim 1. It is suggested that the claim be amended to provide proper antecedent basis.

Claims 7-8 are indefinite in the claim 7, which recites the limitation "the number of the immobilized probe molecules per spot is of the same order to the lowest number of mRNA molecules of a target gene present in a sample" at the end of claim 7. The recitation is indefinite because the number of probe molecules depends on the amount of target, wherein the target is a separate entity that is not a structural limitation of the claimed carrier. Thus, it is unclear if a carrier having multiple areas of probes thereon would infringe on claim 7 merely because an mRNA sample is prepared that happens to have a number of molecules equal to the number of molecules per spot of the carrier.

Claim 11 is indefinite in the recitation "differ 100 to 1000 times between the maximum and the minimum" at the end of the claim. The recitations of "the maximum" and "the minimum" lack antecedent basis because neither of claims 1-2, upon which claim 11 depends, define a maximum or minimum. In addition, it is unclear what quantity or property "the maximum" of "the minimum" refers to.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-4, 6, 10-12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Keefe (U.S. Patent Application Publication No. US 2002/0004204 A1, published 10 January 2002).

Regarding claim 1, O'Keefe teaches a probe carrier. In a single exemplary embodiment, O'Keefe teaches a carrier in the form of a substrate having a plurality of separate microarrays 90 (Figure 3 and paragraph 0102), wherein each microarray comprises a plurality of spots (paragraph 0062). Each microarray also contains a plurality of identical copies of single probe, which differs form one microarray to the next (paragraph 0102). Thus, each microarray comprises a plurality of spots (i.e., at least two) of the same kinds of probes, but each microarray has different probes.

Regarding claims 2-3, O'Keefe teaches the probe carrier of claim 1.

It is noted that the courts have held that "while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function." *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, "[A]pparatus claims cover what a device *is*, not what a device *does*." *Hewlett-Packard Co. v. Bausch &Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Therefore, the various uses recited in claims 2-3 (e.g., quantification or detection of a target substance) fail to define additional structural elements to the device of claims 2-3. Because O'Keefe teaches the structural elements of claims 2-3, the claims are anticipated by O'Keefe. See MPEP § 2114.

Regarding claim 4, O'Keefe teaches the carrier of claim 2, wherein the plurality of areas are aligned in a first direction, and adjacent areas a separated in a direction vertical to the first direction; namely, Figure 2 shows a plurality of areas 90 linearly aligned in one direction, and a second plurality of areas linearly aligned beneath (i.e., vertically under) the first plurality.

Regarding claim 6, O'Keefe teaches the carrier of claim 1, wherein he probe s a nucleic acid; namely, the probe is a biopolymer (paragraph 0015) in the form of a polynucleotide (paragraph 0007), which is a nucleic acid.

Regarding claim 10, O'Keefe teaches the carrier of claim 1.

It is noted that the courts have stated:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP§ 2113.

Thus, the limitation that the probes be immobilized using an ink jet method are part of the process of making the carrier rather than structural limitations of the carrier. Because O'Keefe teaches the structural elements of the claimed carrier, the claim is anticipated by O'Keefe.

Regarding claim 11, O'Keefe teaches the carrier of claim 2, wherein the number of spots in each area differ 100 to 1000 times between the maximum and the minimum; namely, the number of spots per array is at least 100 and up to 100,000 (paragraph 0063), which includes the range of 100-1000 spots per array.

Regarding claim 12, O'Keefe teaches the carrier of claim 2, wherein the two or more areas have a same area; namely, Figure 2 shows each of the array areas as being the same size.

Regarding claim 14, O'Keefe teaches the carrier of claim 1, wherein the carrier is a plate substrate (paragraph 0056).

10. Claims 1-6, 9-10, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirota et al (U.S. Patent Application Publication No. US 2003/0040107 A1, published 27 February 2003).

Regarding claim 1, Hirota et al teach a probe carrier. In a single exemplary embodiment, Hirota et al teach the probe carrier of Figure 14B, which comprises a plurality of spots. The spots form a microarray of DNA fragments (paragraph 0001), which are probes capable of binding to nucleic acid targets. The spots are in known locations on the carrier because the spots are deposited by an ink-jet system (paragraphs 0030-0031), which requires deposition of the spots at known locations. Figure 14a shows a plurality of different separated areas; namely, the first area is interpreted as the area containing spots 3A1 and 3A2, and the second area is interpreted as the area containing spots 3A3 and 3A4. It is noted that a review of the specification yields no limiting definition of, or any specific structural barriers required for, a "separated area." Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "separated area" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see

MPEP 2111 [R-1]). Hirota et al further teach that in each area probes of the same kind are immobilized as one or more spots and proves of different kinds are not immobilized; namely, spots 3A1 and 3A2 (i.e., the first area) are spots of the same sequence (i.e., DNA fragment), and spots 3A3 and 3A4 (i.e., the second area) are also spots of the same sequence (i.e., DNA fragment; paragraph 0127). Both areas have probes of the same kind in two or more spots.

Regarding claim 2, Hirota et al teach the carrier of claim 1, wherein the carrier is configured to allow quantification of two or more kinds of target substances; namely, the carrier comprising the spots allows quantitative performance (paragraph 0014). In addition, the carrier of Figure 14B further comprises spots 1A1-1A4 in different areas, which have different sequences and thus detect a different target substance.

Regarding claim 3, Hirota et al teach the carrier of claim 2, wherein the amount of probes in the plurality of areas varies respectively depending on a target substance to be detected; namely, the amount of capture (i.e., probe) per unit volume immobilized in the spot varies (paragraph 0031).

As noted above, apparatus claims cover what a device *is*, not what a device *does*. Therefore, the various uses recited in claim 3 (e.g., detection of a target substance) fail to define additional structural elements to the device of claim 3. Because Hirota et al teach the structural elements of claim 3, the claim is anticipated by Hirota et al.

Regarding claim 4, Hirota et al teach the carrier of claim 2, wherein the plurality of areas are aligned in a first direction; namely, from left to right in Figure 14B. Figure

14B further comprised adjacent areas separated in a direction vertical to the first area; namely, a third area containing spots 2A1-2A2 and a fourth area containing spots 2A3-2A4 are aligned above (i.e., vertically with) the first and second areas.

Regarding claim 5, Hirota et al teach the carrier of claim 1.

It is noted that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories,* 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component); Celeritas Technologies Ltd. v. Rockwell International Corp., 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The court held that the prior art anticipated the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). Thus, the teaching of Hirota et al that the amount of nucleic acid **may** be varied (paragraph 0031) encompasses the alternate embodiment wherein the amount of nucleic acid is **not** varied; i.e., the spots have the same amount of nucleic acid therein. See MPEP § 2123 [R-5].

In addition, it is noted that a review of the specification yields no limiting definition of the similarity of amounts encompassed by the phrase "practically equal." Thus, in an alternate embodiment of Hirota et al wherein the different sized spots of Figure 14B

each comprise different amounts of nucleic acids, said different amounts are encompassed by the broadly claimed "practically equal" because the metes and bounds of the phrase "practically equal" are not limited by any statements in the specification. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding amounts that are "practically equal."

Regarding claim 6, Hirota et al teach the carrier of claim 1, wherein the probe is a nucleic acid; namely, the spots are DNA fragments (paragraph 0001). DNA is a nucleic acid.

Regarding claim 9, Hirota et al teach the carrier of claim 1, wherein the amount of probes immobilized varies between different areas; namely, the amount of capture (i.e., probe) per unit volume immobilized in the spot varies (paragraph 0031). Because the amount in each spot varies, the amount in different areas (i.e., of spots) varies.

Regarding claim 10, Hirota et al teach the carrier of claim 1, wherein the probes are immobilized is performed by an ink jet method (paragraphs 0030-0031).

In addition, as noted above, the courts have stated that the patentability of a product does not depend on its method of production. Thus, the limitation that the probes be immobilized using an ink jet method are part of the process of making the carrier rather than structural limitations of the carrier. Because Hirota et al teach the structural elements of the claimed carrier, the claim is anticipated by Hirota et al.

Regarding claim 12, Hirota et al teach the carrier of claim 2. As noted above, a review of the specification yields no limiting definition of, or any specific structural barriers required for, a "separated area." The carrier of Figure 14B can therefore be

subdivided into first and second areas of equal total area wherein the first area of the carrier includes spots 3A1 and 3A2 and a surrounding area that does not overlap with the second area of the carrier, which includes spots 3A3 and 3A4 and a surrounding area that does not overlap with the first area of the carrier. Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "separated area"

Regarding claim 14, Hirota et al teach the carrier of claim 1, wherein the carrier is a plate substrate; namely, the array is on a base plate (Abstract).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 5, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Keefe (U.S. Patent Application Publication No. US 2002/0004204 A1, published 10 January 2002) in view of Hirota et al (U.S. Patent Application Publication No. US 2003/0040107 A1, published 27 February 2003).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiments of dependent claims 5 and 9.

Regarding claim 5, O'Keefe teaches the probe carrier of claim 1. In a single exemplary embodiment, O'Keefe teaches a carrier in the form of a substrate having a plurality of separate microarrays 90 (Figure 3 and paragraph 0102), wherein each microarray comprises a plurality of spots (paragraph 0062). Each microarray also contains a plurality of identical copies of single probe, which differs form one microarray to the next (paragraph 0102). Thus, each microarray comprises a plurality of spots (i.e., at least two) of the same kinds of probes, but each microarray has different probes.

O'Keefe does not teach the number of probe molecules per spot is practically equal among all kinds of probes.

However, Hirota et al teach a probe carrier; namely, the carrier of Figure 14B.

As noted above, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Thus, the teaching of Hirota et al that the amount of nucleic acid **may** be varied (paragraph 0031) encompasses the alternate embodiment wherein the amount of nucleic acid is **not** varied; i.e., the spots have the same amount of nucleic acid therein.

In addition, it is noted that a review of the specification yields no limiting definition of the similarity of amounts encompassed by the phrase "practically equal." Thus, in an alternate embodiment of Hirota et al wherein the different sized spots of Figure 14B each comprise different amounts of nucleic acids, said different amounts are encompassed by the broadly claimed "practically equal" because the metes and bounds of the phrase "practically equal" are not limited by any statements in the specification.

Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding amounts that are "practically equal."

Hirota et al also teaches the spots have the added advantage of being applicable by an ink-jet system, which allows the amount per spot to be varied without changing the size of the spot (paragraph 0032). Thus, Hirota et al teach the known technique of having the number of probe molecules per spot practically equal among all kinds of probes.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different probes for different targets immobilized in each spot as taught by O'Keefe so that the number of probe molecules per spot practically equal among all kinds of probes as taught by Hirota et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of having spots that are applicable by an ink-jet system, which allows the amount per spot to be varied without changing the size of the spot as explicitly taught by Hirota et al (paragraph 0032). In addition, it would have been obvious to the ordinary artisan that the known technique of having the number of probe molecules per spot practically equal among all kinds of probes as taught by Hirota et al could have been applied to each spot of the carrier of O'Keefe with predictable results because the known technique of having the number of probe molecules per spot practically equal

among all kinds of probes as taught by Hirota et al predictably results in a carrier suitable for nucleic acid assays.

Regarding claim 9, the carrier of claim 1 is discussed above.

O'Keefe does not explicitly teach the amount of probes immobilized varies between different areas.

However, Hirota et al teach a probe carrier in the form of Figure 14B, wherein the amount of probes immobilized varies between different areas; namely, the amount of capture (i.e., probe) per unit volume immobilized in the spot varies (paragraph 0031). Because the amount in each spot varies, the amount in different areas (i.e., of spots) varies. Hirota et al also teaches the spots have the added advantage of being applicable by an ink-jet system, which allows the amount per spot to be varied without changing the size of the spot (paragraph 0032). Thus, Hirota et al teach the known technique of having the amount of probes immobilized varied between different areas.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different probes for different targets immobilized in each spot as taught by O'Keefe so that the amount of probes immobilized varied between different areas as taught by Hirota et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of having spots that are applicable by an ink-jet system, which allows the amount per spot to be varied without changing the size of the spot as explicitly taught by Hirota et al

(paragraph 0032). In addition, it would have been obvious to the ordinary artisan that the known technique of having the amount of probes immobilized varied between different areas as taught by Hirota et al could have been applied to each spot of the carrier of O'Keefe with predictable results because the known technique of having the amount of probes immobilized varied between different areas as taught by Hirota et al predictably results in a carrier suitable for nucleic acid assays.

13. Claims 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Keefe (U.S. Patent Application Publication No. US 2002/0004204 A1, published 10 January 2002) in view of Roesl et al (U.S. Patent Application Publication No. US 2002/0106355 A1, published 8 August 2002).

It is noted that this rejection applies to claims 1 and 6 to the extent that they are drawn to the embodiments of dependent claims 7-8.

Regarding claim 7, O'Keefe teaches the probe carrier of claim 1. In a single exemplary embodiment, O'Keefe teaches a carrier in the form of a substrate having a plurality of separate microarrays 90 (Figure 3 and paragraph 0102), wherein each microarray comprises a plurality of spots (paragraph 0062). Each microarray also contains a plurality of identical copies of single probe, which differs form one microarray to the next (paragraph 0102). Thus, each microarray comprises a plurality of spots (i.e., at least two) of the same kinds of probes, but each microarray has different probes.

O'Keefe also teaches the carrier of claim 6, wherein the probe is a nucleic acid; namely, the probe is a biopolymer (paragraph 0015) in the form of a polynucleotide (paragraph 0007), which is a nucleic acid.

O'Keefe does not explicitly teach that the number of probe molecules is of the same order to the lowest number of mRNA molecules of a target gene present in a sample.

However, Roesl et al teach a carrier in the form of a nitrocellulose strip wherein equal amounts (i.e., counts) of nascent mRNA is hybridized the same amount of probes on the strip (Figure 2 and paragraphs 0033 and 0066). It is noted that a review of the specification yields no limiting definition of the range of values encompassed by the term "of the same order." Thus, the equal amounts of immobilized probe and the nascent mRNA as taught by Roesl et al are interpreted as being "of the same order," and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "of the same order." Roesl et al also teach the hybridization of equal amounts of the immobilized probe and the mRNA in the sample has the added advantage of allowing direct comparison of the degree of transcription (i.e., mRNA production) of the gene of interest with other genes in the sample (paragraph 0066). Thus, Roesl et al teach the known technique of having the amount of immobilized probes of the same order as the lowest number of mRNA molecules in the sample.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different

probes for different targets immobilized in each spot as taught by O'Keefe so that the amount of each probe in each spot is of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing direct comparison of the degree of transcription (i.e., mRNA production) of the gene of interest with other genes in the sample (paragraph 0066) as explicitly taught by Roesl et al (paragraph 0066). In addition, it would have been obvious to the ordinary artisan that the known technique of having the amount of each probe of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al could have been applied to each spot of the carrier of O'Keefe with predictable results because the known technique of having the amount of each probe of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al predictably results in a probe ratio allowing the testing of regulation of gene expression.

Regarding claim 8, the carrier of claim 7 is discussed above. O'Keefe teaches number of spots in each of the areas in proportional to an average amount of expression, in a human, of the target gene having a sequence complementary to the probe; namely, each area has at least 2 spots. The claim does not define a specific ratio for the claimed proportion. In addition, a review of the specification yields no limiting definition of a range of number encompassed by the phrase "is proportional to." Thus, because the average amount of expression of a target gene can be divided by a

number such that the ratio of 2, the at least two spots of O'Keefe are proportional to an average amount of expression, in a human, of the target gene having a sequence complementary to the probe, and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding amounts that are "proportional to."

14. Claims 1-2 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Keefe (U.S. Patent Application Publication No. US 2002/0004204 A1, published 10 January 2002) in view of Iwaki et al (U.S. Patent Application Publication No. US 2002/0039742 A1, issued 4 April 2002).

It is noted that this rejection applies to claims 1-2 to the extent that they are drawn to the embodiment of dependent claim 11.

Regarding claim 11, O'Keefe teaches the probe carrier of claim 1. In a single exemplary embodiment, O'Keefe teaches a carrier in the form of a substrate having a plurality of separate microarrays 90 (Figure 3 and paragraph 0102), wherein each microarray comprises a plurality of spots (paragraph 0062). Each microarray also contains a plurality of identical copies of single probe, which differs form one microarray to the next (paragraph 0102). Thus, each microarray comprises a plurality of spots (i.e., at least two) of the same kinds of probes, but each microarray has different probes.

O'Keefe also teaches the carrier of claim 2; namely, because the various uses recited in claim 2 (e.g., quantification or detection of a target substance) fail to define

additional structural elements to the device of claim 2. Because the prior art teaches the structural elements of claim 2, the claims are obvious over the prior art.

O'Keefe does not teach each individual array (i.e., area) has 100 to 1000 spots.

However, Iwaki et al teach arrays of nucleic acids spots (Abstract) wherein the probe molecules present in different spots are the same (paragraph 0069), and wherein each array has several hundreds (i.e., 100 to 1000) spots (paragraph 0072). Thus, Iwaki et al teach the known technique of providing hundreds of identical spots within an individual array.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the probe carrier, which comprises a plurality of individual arrays (i.e., the areas of the instant claim) that have multiple spots of the same probes as taught by O'Keefe so that each area (i.e., individual array) has several hundred spots of the same probe molecule as taught by Iwaki et al to arrive at the instantly claimed carrier with a reasonable expectation of success. It would have been obvious to the ordinary artisan that the known technique having several hundred spots of the same probe molecule per area as taught by Iwaki et al could have been applied to each of the areas of O'Keefe with predictable results because the known technique of having several hundred spots of the same probe molecule per area as taught by Iwaki et al predictably results in a carrier having a number of spots useful for analysis of DNA targets.

15. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Keefe (U.S. Patent Application Publication No. US 2002/0004204 A1, published 10 January 2002) in view of Yamamoto et al (U.S. Patent Application Publication No. US 2002/0147330 A1, published 10 October 2002).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiment of dependent claim 13.

Regarding claim 13, O'Keefe teaches the probe carrier of claim 1. In a single exemplary embodiment, O'Keefe teaches a carrier in the form of a substrate having a plurality of separate microarrays 90 (Figure 3 and paragraph 0102), wherein each microarray comprises a plurality of spots (paragraph 0062). Each microarray also contains a plurality of identical copies of single probe, which differs form one microarray to the next (paragraph 0102). Thus, each microarray comprises a plurality of spots (i.e., at least two) of the same kinds of probes, but each microarray has different probes.

O'Keefe does not teach the carrier is a tape.

However, Yamamoto et al teach a probe carrier in the form of a tape, which has the added advantage of having improved efficiency in the manufacturing of the probe carrier (i.e., the deposition of the probes on the carrier; Abstract). Thus, Yamamoto et al teach the known technique of using a tape as a probe carrier.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the probe carrier as taught by O'Keefe so that the carrier substrate is a tape as taught by Yamamoto et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary

artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of having improved efficiency the deposition of the probes on the carrier, thus resulting in improved efficiency in the manufacturing of the probe carrier, as explicitly taught by Yamamoto et al (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using the tape carrier of Yamamoto et al could have been used as the substrate in the carrier of O'Keefe with predictable results because the known technique of using the tape carrier of Yamamoto et al predictably results in a carrier useful for DNA probe arrays.

16. Claims 1 and 6-8 rejected under 35 U.S.C. 103(a) as being unpatentable over Hirota et al (U.S. Patent Application Publication No. US 2003/0040107 A1, published 27 February 2003) in view of Roesl et al (U.S. Patent Application Publication No. US 2002/0106355 A1, published 8 August 2002).

It is noted that this rejection applies to claims 1 and 6 to the extent that they are drawn to the embodiments of dependent claims 7-8.

Regarding claim 7, Hirota et al teach the probe carrier of claim 1. In a single exemplary embodiment, Hirota et al teach the probe carrier of Figure 14B, which comprises a plurality of spots. The spots form a microarray of DNA fragments (paragraph 0001), which are probes capable of binding to nucleic acid targets. The spots are in known locations on the carrier because the spots are deposited by an ink-jet system (paragraphs 0030-0031), which requires deposition of the spots at known

locations. Figure 14a shows a plurality of different separated areas; namely, the first area is interpreted as the area containing spots 3A1 and 3A2, and the second area is interpreted as the area containing spots 3A3 and 3A4. It is noted that a review of the specification yields no limiting definition of, or any specific structural barriers required for, a "separated area." Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "separated area." Hirota et al further teach that in each area probes of the same kind are immobilized as one or more spots and proves of different kinds are not immobilized; namely, spots 3A1 and 3A2 (i.e., the first area) are spots of the same sequence (i.e., DNA fragment), and spots 3A3 and 3A4 (i.e., the second area) are also spots of the same sequence (i.e., DNA fragment; paragraph 0127). Both areas have probes of the same kind in two or more spots.

Hirota et al teach the carrier of claim 6, wherein the probe is a nucleic acid; namely, the spots are DNA fragments (paragraph 0001). DNA is a nucleic acid.

Hirota et al do not explicitly teach that the number of probe molecules is of the same order to the lowest number of mRNA molecules of a target gene present in a sample.

However, Roesl et al teach a carrier in the form of a nitrocellulose strip wherein equal amounts (i.e., counts) of nascent mRNA is hybridized the same amount of probes on the strip (Figure 2 and paragraphs 0033 and 0066). It is noted that a review of the specification yields no limiting definition of the range of values encompassed by the term "of the same order." Thus, the equal amounts of immobilized probe and the

nascent mRNA as taught by Roesl et al are interpreted as being "of the same order," and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "of the same order." Roesl et al also teach the hybridization of equal amounts of the immobilized probe and the mRNA in the sample has the added advantage of allowing direct comparison of the degree of transcription (i.e., mRNA production) of the gene of interest with other genes in the sample (paragraph 0066). Thus, Roesl et al teach the known technique of having the amount of immobilized probes of the same order as the lowest number of mRNA molecules in the sample.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the carrier having different probes for different targets immobilized in each spot as taught by Hirota et al so that the amount of each probe in each spot is of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of allowing direct comparison of the degree of transcription (i.e., mRNA production) of the gene of interest with other genes in the sample (paragraph 0066) as explicitly taught by Roesl et al (paragraph 0066).

In addition, it would have been obvious to the ordinary artisan that the known technique of having the amount of each probe of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al could have

been applied to each spot of the carrier of Hirota et al with predictable results because the known technique of having the amount of each probe of the order of the lowest number of molecules or mRNA complementary to the probe as taught by Roesl et al predictably results in a probe ratio allowing the testing of regulation of gene expression.

Regarding claim 8, the carrier of claim 7 is discussed above. Hirota et al teach number of spots in each of the areas in proportional to an average amount of expression, in a human, of the target gene having a sequence complementary to the probe; namely, each area has 2 spots. The claim does not define a specific ratio for the claimed proportion. In addition, a review of the specification yields no limiting definition of a range of number encompassed by the phrase "is proportional to." Thus, because the average amount of expression of a target gene can be divided by a number such that the ratio of 2, the two spots of Hirota et al are proportional to an average amount of expression, in a human, of the target gene having a sequence complementary to the probe, and the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding amounts that are "proportional to."

17. Claims 1-2 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirota et al (U.S. Patent Application Publication No. US 2003/0040107 A1, published 27 February 2003) in view of Iwaki et al (U.S. Patent Application Publication No. US 2002/0039742 A1, issued 4 April 2002).

It is noted that this rejection applies to claims 1-2 to the extent that they are drawn to the embodiment of dependent claim 11.

Regarding claim 11, Hirota et al teach the probe carrier of claim 1. In a single exemplary embodiment, Hirota et al teach the probe carrier of Figure 14B, which comprises a plurality of spots. The spots form a microarray of DNA fragments (paragraph 0001), which are probes capable of binding to nucleic acid targets. The spots are in known locations on the carrier because the spots are deposited by an ink-jet system (paragraphs 0030-0031), which requires deposition of the spots at known locations. Figure 14a shows a plurality of different separated areas; namely, the first area is interpreted as the area containing spots 3A1 and 3A2, and the second area is interpreted as the area containing spots 3A3 and 3A4. It is noted that a review of the specification yields no limiting definition of, or any specific structural barriers required for, a "separated area." Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "separated area." Hirota et al further teach that in each area probes of the same kind are immobilized as one or more spots and proves of different kinds are not immobilized; namely, spots 3A1 and 3A2 (i.e., the first area) are spots of the same sequence (i.e., DNA fragment), and spots 3A3 and 3A4 (i.e., the second area) are also spots of the same sequence (i.e., DNA fragment; paragraph 0127). Both areas have probes of the same kind in two or more spots.

Hirota et al also teach the carrier of claim 2, wherein the carrier is configured to allow quantification of two or more kinds of target substances; namely, the carrier comprising the spots allows quantitative performance (paragraph 0014). In addition, the

carrier of Figure 14B further comprises spots 1A1-1A4 in different areas, which have different sequences and thus detect a different target substance.

For the purpose of examination, Figure 14B of Hirota et al is interpreted as a macro array comprising individual arrays, wherein the individual arrays are the areas of the instant claim.

Hirota et al do not teach each individual array (i.e., area) has 100 to 1000 spots.

However, Iwaki et al teach arrays of nucleic acids spots (Abstract) wherein the probe molecules present in different spots are the same (paragraph 0069), and wherein each array has several hundreds (i.e., 100 to 1000) spots (paragraph 0072). Thus, Iwaki et al teach the known technique of providing hundreds of identical spots within an individual array.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the probe carrier, which comprises a plurality of individual arrays (i.e., the areas of the instant claim) that have multiple spots of the same probe molecules as taught by Hirota et al so that each area (i.e., individual array) has several hundred spots of the same probe molecule as taught by Iwaki et al to arrive at the instantly claimed carrier with a reasonable expectation of success. It would have been obvious to the ordinary artisan that the known technique having several hundred spots of the same probe molecule per area as taught by Iwaki et al could have been applied to each of the areas of Hirota et al with predictable results because the known technique of having several hundred spots of the same probe

molecule per area as taught by Iwaki et al predictably results in a carrier having a number of spots useful for analysis of DNA targets.

18. Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirota et al (U.S. Patent Application Publication No. US 2003/0040107 A1, published 27 February 2003) in view of Yamamoto et al (U.S. Patent Application Publication No. US 2002/0147330 A1, published 10 October 2002).

It is noted that this rejection applies to claim 1 to the extent that it is drawn to the embodiment of dependent claim 13.

Regarding claim 13, Hirota et al teach the probe carrier of claim 1. In a single exemplary embodiment, Hirota et al teach the probe carrier of Figure 14B, which comprises a plurality of spots. The spots form a microarray of DNA fragments (paragraph 0001), which are probes capable of binding to nucleic acid targets. The spots are in known locations on the carrier because the spots are deposited by an ink-jet system (paragraphs 0030-0031), which requires deposition of the spots at known locations. Figure 14a shows a plurality of different separated areas; namely, the first area is interpreted as the area containing spots 3A1 and 3A2, and the second area is interpreted as the area containing spots 3A3 and 3A4. It is noted that a review of the specification yields no limiting definition of, or any specific structural barriers required for, a "separated area." Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding a "separated area." Hirota et al further teach that in each area probes of the same kind are

immobilized as one or more spots and proves of different kinds are not immobilized; namely, spots 3A1 and 3A2 (i.e., the first area) are spots of the same sequence (i.e., DNA fragment), and spots 3A3 and 3A4 (i.e., the second area) are also spots of the same sequence (i.e., DNA fragment; paragraph 0127). Both areas have probes of the same kind in two or more spots.

Hirota et al also teach the carrier of claim 2, wherein the carrier is configured to allow quantification of two or more kinds of target substances; namely, the carrier comprising the spots allows quantitative performance (paragraph 0014). In addition, the carrier of Figure 14B further comprises spots 1A1-1A4 in different areas, which have different sequences and thus detect a different target substance.

Hirota et al do not teach the carrier is a tape.

However, Yamamoto et al teach a probe carrier in the form of a tape, which has the added advantage of having improved efficiency in the manufacturing of the probe carrier (i.e., the deposition of the probes on the carrier; Abstract). Thus, Yamamoto et al teach the known technique of using a tape as a probe carrier.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the probe carrier as taught by Hirota et al so that the carrier substrate is a tape as taught by Yamamoto et al to arrive at the instantly claimed carrier with a reasonable expectation of success. The ordinary artisan would have been motivated to make the modification because said modification would have resulted in a carrier having the added advantage of having improved efficiency the deposition of the probes on the carrier, thus resulting in improved

efficiency in the manufacturing of the probe carrier, as explicitly taught by Yamamoto et al (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using the tape carrier of Yamamoto et al could have been used as the substrate in the carrier of Hirota et al with predictable results because the known technique of using the tape carrier of Yamamoto et al predictably results in a carrier useful for DNA probe arrays.

Conclusion

19. No claim is allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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